REMARKS

Reconsideration is requested.

Claims 1-10 are pending. Claim 10 has been withdrawn from consideration.

Claim 5 has been canceled above, without prejudice. Claims 1-4 and 6-10 will be pending upon entry of the present Amendment. Entry of the present Amendment is requested to advance prosecution.

The Section 103 rejection of claims 1-5, 8 and 9 over Sen (1997, Oncogene, 14, pp 2195-2200) "as evidenced by" Entrez Gene (AURKA Aurora Kinase A, Last Accessed 06/03/2010, http://www.ncbi.nlm.nih.gov/sites/entrez/?db=gene&cmd=Retrieve&dopt=summary&list_uids=8465) and in view of Patel (2000, Oncogene, 19, pp 4159-4169) and Hauf (2003, Journal of Cell Biology, Vol. 161, No. 2, pp-281-294) is traversed. Reconsideration and withdrawal of the rejection is requested in view of the evidence of record and the following further comments.

The Examiner relies on Hauf for an alleged teaching that

> "Hesperadin is an aurora A kinase inhibitor (see entire document, for instance page 284, column 2, last paragraph). Hauf proffers that Hesperadin treatment turned off checkpoint signaling in Taxol-treated cells because all kinetochores progressively accumulated stably attached microtubles. Hauf teaches that Hesperadin might allow cells treated with paclitaxel to exit the mitotic phase by stabilizing improper microtubule attachments (see entire document, for instance page 288, column 2, last sentence).

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the antineoplastic agent paclitaxel of Patel and the aurora A kinase inhibitor Hesperadin of Hauf to treat a patient with breast cancer, such as those of Sen." See page 4 of the Office Action dated January 14, 2011

In fact, Hauf teaches that Hesperadin is an Aurora B kinase inhibitor. See for example, page 282, left column of the reference ("Our data indicate that the mitotic effects of this compound, which we call Hesperadin, are due to inhibition of Aurora B function"); page 283, right column of the reference ("**Hesperadin inhibits Aurora B function**", "Hesperadin appears to inhibit Aurora B function", and "These findings further indicate that Hesperadin inhibits Aurora B and imply that Aurora B function is also required for central spindle assembly in human cells."); page 284, left column of the reference ("We conclude that Hesperadin inhibits Aurora B function in living cells either directly or indirectly."); page 284, right column of the reference ("To further test if the phenotype induced by Hesperadin is due to the inhibition of Aurora B function, we used RNA interference (RNAi)."); the sentence spanning pages 284-285 of the reference ("Hesperadin-treated cells exhibit a very similar phenotype (Figs. 1 and 2), which is further evidence that Hesperadin inhibits Aurora B function in vivo."); page 285, left column of the reference ("To investigate the role of Aurora B in chromosome segregation, we performed chromosome spreading of mitotic HeLa cells treated with Hesperadin."); page 286, left column ("These observations indicate that the defect in chromosome segregation induced by Hesperadin can be specifically ascribed to the inhibition of Aurora B function during the process of chromosome attachment."); and

page 288, right column of the reference ("The number of Mad2-positive kinetochores decreased from 6.3 (range 3-9; *n* = 12 cells) in monastrol-treated control cells to 1.2 (range 0-5; *n* = 25 cells) after 1 h of Hesperadin treatment, indicating that inhibition of Aurora B function might indeed stabilize syntelic attachments.").

Accordingly, contrary to the Examiner's assertion, Hauf does not teach "Hesperadin is an aurora A kinase inhibitor". The cited reference teaches that Hesperadin is an Aurora B kinase inhibitor.

One of ordinary skill in the art will appreciate that Hauf describes Hesperadin as an Aurora B kinase inhibitor. Evidence of same is found in the attached Stolz et al[1] that refers to Hauf in describing hesperadin (and ZM447439) as a "selective Aurora-B inhibitors". See page 3882, sentence spanning left and right columns, of Stolz et al.

While the combination of Patel and Hauf may have made it obvious to utilize the antineoplastic agent paclitaxel or Patel and the Aurora B kinase inhibitor Hesperadin of Hauf, which the applicants do not admit to be the case, the combination of cited art would not have made it obvious to have used an Aurora A kinase inhibitor in a manner required by the presently claimed invention.

The combination of cited art would not have made the claimed invention obvious as, for example, the cited art fails to teach or suggest the use of an Aurora A kinase inhibitor in the manner claimed.

Withdrawal of the Section 103 rejection is requested.

Further, the presently claimed invention requires use of an Aurora A kinase inhibitor in connection with compounds such as Taxol (i.e., mitotic spindle assembly inhibitors), such as the applicants described in Anand et al.[2] ("SIGNIFICANCE … Our findings have important implications for cancer chemotherapy. They suggest that AURORA-A amplification will predict poor responsiveness to Taxol and other agents that target the spindle checkpoint. If so, inhibitors of Aurora-A activity may be a valuable adjunct to these agents in the treatment of cancers that overexpress AURORA-A.").

The applicants have previously antedated Hauf, by reference to Anand et al. See the Rule 131 Declaration filed June 8, 2009.

The Examiner has previously found the Declaration "unpersuasive" to antedate Hauf - asserting that Anand et al

> "does not provide sufficient teaching for the invention as currently claimed. Applicant is currently claiming a combination of taxol and Aurora kinase inhibitor, which is taught by Hauf et al, whereas Anand et al, while being directed to the mitotic spindle assembly inhibitor paclitaxel, does not teach the use of Aurora kinase inhibitors. Anand et al rather addresses the negative effects associated with Aurura-A over-expression by utilizing *BUB1* which affects the spindle checkpoint which the Aurura-A is having a negative effect upon, rather than inhibiting Aurura kinase. Therefore, Applicant's arguments are not found persuasive since Anand et al is not teaching the same invention/combination as either Hauf et al or the instantly claimed invention." See pages 3-4 of the Office Action dated October 14, 2009.

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[1] "Pharmacologic Abrogation of the Mitotic Spindle Checkpoint by an Indolocarbazole Discovered by Cellular Screening Efficiently Kills Cancer Cells" Cancer Res 2009; 69(9), May 1, 2009.

[2] "AURORA-A amplification overrides the mitotic spindle assembly checkpoint, inducing resistance to Taxol" Cancer Cell, January 2003, volume 3, pp 51-62).

As Hauf does not describe or suggest the use of an Aurora A kinase inhibitor, as presently claimed, but rather teaches away from the claimed invention in the use of (at best) an Aurora B kinase inhibitor, Anand et al is sufficient to establish invention of the subject matter of the rejected claims prior to the effective date of the reference, at least to the extent the Examiner believes to be taught in Hauf and certainly to any extent actually suggested by Hauf.

The Examiner has previously appreciated that Anand et al describes aspects of the disclosed invention. Specifically, the Examiner stated as follows on page 5 of the Office Action dated February 6, 2009 (underlined emphasis added):

> "Said combination of paclitaxel and heperadin would have an effect on breast cancer cells. This is evidenced by Anand teaching that paclitaxel functions to treat breast cancer by causing the cells to proceed to apoptosis (see page 59, first column, last paragraph), and Anand also teaches that AURORA-A over-expression is present in breast cancer (see page 51, "significance") and functions to disrupt the spindle checkpoint that is activated by paclitaxel (see page 59, first column, last paragraph, through second column, first paragraph). This reads on **instant claims 1-5 and 8-9**."

The Examiner has more-recently asserted in the Office Action dated October 14, 2009 that

> "Anand et al … does not teach the use of Aurora kinase inhibitors." See pages 3-4 of the Office Action dated October 14, 2009.

With due respect to the Examiner, the applicants submit that one of ordinary skill in the art will appreciate from Anand et al that the applicants were in possession of the

claimed invention prior to the publication of Hauf. Anand et al describes a new and useful combination in a method of treatment, at least to an extent the Examiner has interpreted Hauf.

The previously-filed Rule 131 Declaration is submitted to be persuasive in antedating the Hauf, to the extent same may be required to obviate the Section 103 rejection.

Withdrawal of the Section 103 rejection is requested.

The Section 103 rejection of claim 6 over Sen "as evidenced by" Entrez Gene, in view of Patel, Hauf and Slamon (New England Journal of Medicine, Vol. 344, No. 11, pp 783-792). Reconsideration and withdrawal of the rejection are requested for reasons noted above with regard to the patentability of claim 1 over Hauf as claim 6 depends from and includes the details of claim 1 and the further teachings of the Examiner's secondary references fail to cure the deficiencies of Hauf.

The Section 103 rejection of claim 7 over Sen "as evidenced by" Entrez Gene, in view of Patel, Hauf and Obermiller (Breast Cancer Research 2000, 2:28-31). Is traversed. Reconsideration and withdrawal of the rejection are requested for reasons noted above with regard to the patentability of claim 1 over Hauf as claim 7 depends from and includes the details of claim 1 and the further teachings of the Examiner's secondary references fail to cure the deficiencies of Hauf.

The claims are submitted to be in condition for allowance. Entry of the present Amendment and a Notice of Allowance are requested. The Examiner is requested to

contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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